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SPLENIC VOLUME CHANGE AND THERAPUETIC RESPONSE IN PATIENTS TREATED WITH RADIOIMMUNOCONJUGATES

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ABSTRACT

Splenomegaly is frequently found in non-Hodgkin's lymphoma (NHL) patients. This study evaluated the implications of splenic volume change in response to radioimmunotherapy (RIT). **Methods:** Twenty-nine NHL patients treated with radiolabeled-Lym-1 and 9 breast cancer patients (reference group) treated with radiolabeled-ChL6, BrE-3 or m170 were analyzed using CT splenic images obtained before and after RIT. Patient-specific radiation doses to spleen were determined using actual splenic volume determined by CT and body weight. **Results:** In 13 of 29 NHL patients who had splenic volume ≤ 310 ml, there was no or small change (-23 to 15 mL) in splenic volume, despite splenic doses as high as 14.4 Gy. Similarly, in a reference group of 9 breast cancer patients, there was no or small change (-5 to 13 mL), despite splenic doses as high as 11.4 Gy. In contrast, 13 of 29 NHL patients who had splenic volume 380-1400 mL, splenic volume decreased by 68 to 548 mL despite splenic doses as low as 1.40 Gy. Ten of 29 NHL patients with greater than a 15% decrease in splenic volume after RIT had nodal tumor regression (5 CR, 5 PR). In the remaining 19 NHL patients with less than a 15% decrease in splenic volume after RIT, there were 7 non-responders (5 CR and 7 PR). **Conclusion:** Splenic volume changes were found in NHL patients with splenomegaly. These splenic volume changes is likely due to therapeutic effect on malignant lymphocytes associated with splenomegaly. Nodal tumor response was more likely when splenomegaly decreased after RIT.

Key Words: Splenomegaly, Radioimmunotherapy, Radiation dosimetry, Lymphoma, Cancer therapy.

INTRODUCTION

Splenomegaly occurs frequently in non-Hodgkin's lymphoma (NHL) patients as a result of NHL infiltration. Associated hypersplenism can cause anemia which needs frequent transfusions, as well as increased susceptibility to infection and bleeding. For radioimmunotherapy (RIT), an enlarged spleen can represent a "sink" to take a large portion of radiolabeled antibody before it is available for nodal tumors. Although splenomegaly is not classified as a tumor burden (1), an enlarged spleen with malignancy is generally associated with poor prognosis. Patients with splenomegaly have been excluded from trials of radioimmunotherapy because they, in general, did not have a "favorable biodistribution" reflected by lower tumor uptake (2,3). However, in treatment of NHL with ^{131}I -Lym-1, although a positive correlation was found between splenic volume and splenic cumulated activity, no correlation was found between initial splenic volume and nodal tumor response (4). Complete response occurred in a patient whose spleen was 970 ml, while there were two non-responders and four partial responders among six patients who had prior splenectomy. Similarly, no correlation was found between splenomegaly and nodal tumor response in NHL patients receiving with ^{90}Y -IDEC-Y2B8 (5).

Although the rationale for excluding patients with splenomegaly from RIT has not been clearly supported by clinical evidences, the benefit of treating patients with splenomegaly has also not been established. Uptake of radiolabeled antibody by an enlarged spleen might be therapeutic for malignant lymphocytes in the spleen. Because we treated patients with splenomegaly, we were able to examine the implications of splenomegaly and change in splenic volume due to RIT. In the present study, changes in splenic volume were examined in NHL patients with and without splenomegaly. As an additional point of comparison, we also measured the spleen sizes of a reference patient group (breast cancer patients) before and after RIT, whose spleen are expected with no malignant involvement. A practical patient-specific splenic dosimetry method was used to account for large deviation for actual spleen volume and body weight from that of reference man (6,7).

MATERIALS AND METHODS

Radiopharmaceuticals

¹³¹I-Lym-1 and ⁶⁷Cu-2IT-BAT-Lym-1. Lym-1 is an IgG_{2a}, mouse monoclonal antibody (MAb) with high affinity for a polymorphic variant of the HLA-DR membrane antigen found on B-cell malignancies (8). Iodine-labeled Lym-1 was prepared using chloramine T at a mass ratio of about 1 mg chloramine T:10 mg Lym-1. Copper-labeled Lym-1 was conjugated with 2IT-BAT for labeling with ⁶⁷Cu (9).

¹³¹I-ChL6 and ¹³¹I-L6. ChL6 is an IgG₁ humanized MAb that binds to adenocarcinomas, including 50% of human breast cancer. ChL6 also mediates antibody-dependant cytotoxicity (10). The radiopharmaceuticals were prepared by chloramine T radioiodination with ¹³¹I and contained 10 mCi ¹³¹I/mg antibody and 1 mCi ¹³¹I/ml solution.

¹¹¹In/⁹⁰Y-MX-DTPA-Bre-3. Bre-3 is a mouse IgG₁ MAb that recognizes an epitope on the tandem repeat of the peptide core of breast mucin (11). Bre-3 binds to 97% of human ductal breast cancer specimen. Bre-3 was provided by Coulter Immunology and conjugated with MX-DTPA for labeling with ¹¹¹In and ⁹⁰Y.

¹¹¹In/⁹⁰Y-2IT-BAD-m170. m-170 is a panadenocarcinoma MAb that reacts with over 90% of human adenocarcinomas, including breast cancers (12). m-170 was provided by Biomira (Canada) and conjugated with 2IT-BAD for labeling with ¹¹¹In and ⁹⁰Y.

Patients

Inclusion Criterion. Spleen volume was determined from CT images. All patients had CT scans before and after RIT, however, in some patients, CT films did not completely cover the spleen volume as these films were prepared previously for the purpose of tumor assessment. In the current retrospective analysis, patients were excluded if they did not have complete CT information for spleen volume

measurements before and after RIT.

NHL patients. At the time of this analysis, 66 NHL patients received ^{131}I -Lym-1 (n=54) (13,14), or ^{67}Cu -2IT-BAT-Lym-1 (n=12) (9,15). All patients had failed combination chemotherapy. Within this group, 29 patients (25 received ^{131}I , 4 received ^{67}Cu) were included because they had abdominal CT films that covered spleen volume before and after RIT (Table 1). Splenic volume change in response to RIT was examined.

Breast cancer patients. At the time of this analysis, 16 breast cancer patients received ^{131}I -ChL6, ^{131}I -L6 (n=11) (10), ^{90}Y -MX-DTPA-Bre-3 (n=4) (11), or ^{90}Y -2IT-BAD-m170 (n=1) (12). All patients had failed combination chemotherapy for metastatic diseases. Within this group, 9 patients (6 received ^{131}I , 3 received ^{90}Y) were included because they had abdominal CT films that covered spleen volume before and after RIT (Table 1). These breast cancer patients served as a reference group for splenic volume change of in response to RIT.

All patients were signed an informed consent for the protocol that was approved by the University of California at Davis Human Subjects and Radiation under an Investigational New Drug authorization from the US Food and Drug Administration.

Splenic Volume and Nodal Tumor Response Assessment

Splenic volume assessment. All patients in the present analysis received multiple doses of RIT (Table 1). The time intervals between the doses were 2 or 4 weeks (9-16). CT scans were acquired 1-3 weeks before RIT, and at least 2 weeks after the last dose of RIT. The average time interval between the last dose injection and the after treatment CT scan was 5 weeks in breast cancer patients and 4 weeks in NHL patients. Transverse CT slices were either 5 or 10-mm in thickness. Splenic volumes were determined using the sum-of-areas method (4,17). The area of spleen region of interest (ROI) on each CT slice was determined by a digitizer and multiplied by the slice thickness to obtain the spleen volume in each slice. All slices were summed to determine the total spleen volume. The accuracy of this method was $3.6 \pm 4.5\%$ (17). A 15% volume change ($> 2\sigma$) after RIT was considered as substantial with a confidence level

high than 98%. Based on definitions by Goldstone (18) and Xiros et al. (19), a splenic volume ≥ 1500 mL is considered as massive splenomegaly, a volume of 500-1499 mL is considered as moderate splenomegaly.

For assessing possible splenic volume change during sequential planar imaging, splenic sizes were measured using planar images. Ten lymphoma patients who had $> 15\%$ CT volume change after RIT were assessed as splenic volume changes during sequential planar imaging were more likely to be detected in those patients. Splenic sizes were measured in the long axis L and the perpendicular short axis W of the spleen silhouette as visualized in planar images acquired immediately and ≥ 120 hours post injection. This approach follows the method described Silverman et al. (20), which demonstrated that spleen size can be estimated from measurements of length and width of the spleen as visualized by a gamma camera after administration of technetium-99m sulfur colloid, with a 1-standard-deviation accuracy of 45g.

Nodal tumor response assessment. Nodal tumors were evaluated by CT or MRI, except for small palpable tumors (14). Nodal tumor masses were evaluated by CT or MRI at a minimum of 1 and 3 months after completion of RIT, and then at a 6-month interval. For small palpable tumors, two perpendicular diameters for each mass were measured using a caliper at each physical examination. Tumor responses were classified as complete response (CR), the complete absence of demonstrable disease, including negative bone marrow examination, or partial response (PR), a decrease in the sum of the products of all tumor dimensions by at least 50% or all tumor volumes by at least 70%. The remaining patients were classified as non-responder (NR).

Radiation Dosimetry

Planar image quantification for the spleen has been previously described (4,21,22). Briefly, planar conjugate views for whole body and abdomen were acquired with a Siemens Bodyscan dual-head camera or an Orbitor single-head camera (Siemens Medical System, Inc., Des Plaines, IL). A high-energy

collimator was used for ^{131}I and a medium energy collimator was used for ^{67}Cu and ^{111}In . Serial images of conjugate views were acquired immediately, 4-6 hours and daily up to 144-264 hours post administration of radiolabeled antibodies. All sequential images were displayed for selecting one image that had best image contrast for spleen. A single reference spleen ROI was determined from that image and this single ROI was mapped to the spleen in all sequential images. The amount of radioactivity in spleen and body were determined by converting counts in spleen and body ROI using geometric-mean quantification. Cumulated activity and biological half-life of the spleen and body were determined by fitting pharmacokinetic data to a mono-exponential curve. Cumulated ^{90}Y activity was derived from that of ^{111}In assuming they had identical uptakes (11).

For an effective clearance half-life of 18 hour (23), 99% of the radiation dose to the spleen was absorbed within 120 hours post injection. There was no or small spleen size change during sequential planar imaging (see Results), spleen volume was considered as a constant or adjusted for a measured small change in dose calculation. Radiation dose to spleen was calculated using a practical, patient-specific approach (24)

$$D_{\text{spleen}} = \tilde{A}_{\text{spleen}} \cdot S(\text{spleen} \leftarrow \text{spleen}) + (\tilde{A}_{\text{TB}} - \tilde{A}_{\text{spleen}}) \cdot S(\text{spleen} \leftarrow \text{RB}) \quad \text{Eq.1}$$

where $\tilde{A}_{\text{spleen}}$ and \tilde{A}_{TB} were cumulated radioactivity in spleen and total body; $S(\text{spleen} \leftarrow \text{spleen})$ and $S(\text{spleen} \leftarrow \text{RB})$ were S values from spleen to spleen and from the remainder of the body to spleen. $S(\text{spleen} \leftarrow \text{RB})$ equals zero for the pure beta emitter, ^{90}Y (6). For ^{131}I and ^{67}Cu (25)

$$S(\text{spleen} \leftarrow \text{RB}) = S(\text{spleen} \leftarrow \text{TB}) \cdot \frac{m_{\text{TB}}}{m_{\text{RB}}} - S(\text{spleen} \leftarrow \text{spleen}) \cdot \frac{m_{\text{spleen}}}{m_{\text{RB}}} \quad \text{Eq. 2}$$

where m_{TB} was the patient-specific body weight; m_{spleen} was determined from the CT volume assuming 1 g/mL; m_{RB} was the difference between m_{TB} and m_{spleen} ; $S(\text{spleen} \leftarrow \text{TB})$ was S value from total body to spleen. Patient-specific $S(\text{spleen} \leftarrow \text{TB})$ was calculated as $1.07 \cdot S(\text{TB} \leftarrow \text{TB})$ for ^{131}I and $1.04 \cdot S(\text{TB} \leftarrow \text{TB})$ for ^{67}Cu (see last paragraph of DISCUSSION). Patient-specific $S(\text{TB} \leftarrow \text{TB})$ was calculated according to MIRD schema (26):

$$S(TB \leftarrow TB) = \frac{1}{m_{TB}} \cdot [\sum \Delta_p \cdot \phi_p(TB \leftarrow TB) + \sum \Delta_{np}] \quad \text{Eq. 3}$$

where Δ_p and Δ_{np} were equilibrium dose constant for each penetrating (p) and non-penetrating (np) radiation energy; $\phi_p(TB \leftarrow TB)$ was the absorbed fraction for each penetrating radiation energy for the total body. The value of $\phi_p(TB \leftarrow TB)$ for each photon energy was calculated with logarithmic interpolation of listed photon energies (20- 2750 keV) and body masses (40-200 kg) in the MIRD table (27,28). Similarly, patient-specific $S(\text{spleen} \leftarrow \text{spleen})$ was calculated as:

$$S(\text{spleen} \leftarrow \text{spleen}) = \frac{1}{m_{TB}} \cdot [\sum \Delta_p \cdot \phi_p(\text{spleen} \leftarrow \text{spleen}) + \sum \Delta_{np}] \quad \text{Eq. 4}$$

where the value of $\phi_p(\text{spleen} \leftarrow \text{spleen})$ for each photon energy was calculated with logarithmic interpolation of listed photon energies (20 – 2750 keV) and target masses (40- 6000 g) in MIRD tables (27-29). The above computations were implemented using a software program developed in-house on a PC computer.

RESULTS

Splenic Volume Change and Nodal Tumor Response

Splenic volume changes after RIT were found in the NHL patients. Although there was no correlation between splenic volume change and radiation absorbed dose to the spleen, splenic volume changes was more likely in patients with enlarged spleen (Fig 1). In 13 of 29 NHL patients who had initial splenic volumes of 150-310 ml, splenic volume changed 0% (range –9 to 7%) despite radiation doses to the spleen as large as 11.4 Gy (Table 2). Similarly, in 9 breast cancer patients who had initial splenic volume of 70-340 mL, splenic volume changed 0% (range –4 to 5%) despite radiation doses to the spleen as large as 14.4 Gy. In contrast, in the 13 of 29 NHL patients who had spleens volume of 380-1400 ml, splenic volumes decreased by 28% (range 12-57%) after receiving a splenic dose as low as 1.40 Gy. In the

remaining 3 NHL patients who had initial splenic volume of 340-700 mL, splenic volume increased by 8, 10 and 220% after RIT. The patient with 220% splenic volume increase had progressive tumor growth after RIT (non-responder).

There was no clear relationship between tumor response and initial splenic volume. However, tumor response was more likely in those patients with greater splenic volume decrease after RIT (Fig 2). Ten of 29 NHL patients with > 15% splenic volume decrease all had nodal tumor regression (5 CR, 5 PR). In the remaining 19 NHL patients with < 15% splenic volume decrease, there were 7 non-responders (5 CR, 7 PR).

Radiation Dosimetry

In 10 of 29 NHL patients who had splenic CT volume change > 15%, mean splenic volume change during sequential imaging were 3.8% (range -2.9 to 10.2) (Table 3). Although 144 hour was the last imaging time point for patient No.9, image at day 72 hours post injection was used for splenic volume measurement as spleen image contrast became poor after 96 hours. This patient had effective clearance half life of 15.5 hour for the spleen, 96% radiation dose was deposited to the spleen during 72 hours. Spleen volume was adjusted by 3.5% (an average for 7.0%) for patient 3, 3.7% for patient 4, 4.4% for patient 7, and 5.1% for patient 8. For the remaining 25 NHL patients, splenic volume was considered to be constant in splenic dose calculation.

Splenic volume ranged from 140 to 2240 mL in 29 NHL patients and from 70 to 340 mL in 9 breast cancer patients (Table 4). Consequently, the calculated radiation dose to spleen using the $S(\text{spleen} \leftarrow \text{spleen})$ values from MIRD reference man (174 g)(6) would be underestimated or overestimated for individual patients. The patient-specific $S(\text{spleen} \leftarrow \text{spleen})$ value decreased as the spleen mass increased (Fig 3.). In 25 NHL patients that received ^{131}I -Lym-1, spleen dose contribution from radioactivity in spleen would have been overestimated by a factor of 10 if the $S(\text{spleen} \leftarrow \text{spleen})$ value from MIRD reference man was used for a patient whose spleen volume was 2240 mL.

As a secondary but still significant effect, body weights ranged from 49 kg to 146 kg in 29 NHL and 9 breast cancer patients (Table 3). The calculated radiation dose to body, using the $S(TB \leftarrow TB)$ values from MIRD mathematical phantom of reference man (69.88 kg)(6), would be underestimated or overestimated for individual patients. Patient-specific $S(TB \leftarrow TB)$ value decreased as body weight increased. In 25 NHL patients that received ^{131}I -Lym-1, deviation in body dose ranged from 27% underestimation for a patient who weighed 49 kg to 96% overestimation for a patient who weighed 146 kg, if the $S(TB \leftarrow TB)$ values of MIRD phantom were used.

DISCUSSION

The spleen consists of red pulp (containing abundant erythrocytes and venous sinuses), white pulp (containing mainly lymphocytes), and connective tissues. As erythrocytes, venous sinuses, and connective tissues are relatively radiation-resistant, only white pulp in spleen is radiation-sensitive. In the present analysis, we observed in 13 NHL patients who had splenic volumes of 150-310, the change in splenic volume ranged -9 to 7% despite radiation dose to spleen as high as 11.4 Gy (Table 2). Similarly, in a reference group of 9 breast cancer patients who had initial splenic volume of 70-340 mL, splenic volume changed -4 to 5%, despite radiation doses to the spleen as large as 14.4 Gy. These observations are in agreement with other reports of no measurable change in splenic size (30) and functional impairment (31) for dose up to 18 Gy. All these observations are consistent with the fact that the radiosensitive white pulp represents only a small portion of total splenic volume (white pulp represents 6.3-8.3 % of the reference adult spleen)(32).

Splenic volume changes after RIT were found in NHL patients who had enlarged spleens, a condition wherein NHL involvement is more likely. In 28 NHL patients who had a spleen mass greater than 500 g and underwent splenectomy, Xiros et al found 27 patients (96%) had spleen NHL involvement

(19). In the present study, 13 of the 29 NHL patients with spleen volume of 380-1400 ml had splenic volume decreases by 70-550 mL associated with a low splenic dose (Table 2). Differential results in normal-sized and enlarged spleens suggests that the decrease in splenic volumes after RIT in the above dose range is likely due to therapeutic effect on malignant lymphocytes associated with splenomegaly. Because an enlarged spleen commonly represents a poor prognostic indicator of itself, splenectomy is often performed in NHL patients with substantial splenomegaly. For patients without splenectomy, a large splenic uptake of radiolabeled antibody is therapeutic for malignant lymphocytes in the spleen. This is consistent with the treatment of chronic lymphocytic leukemia (CLL) and Hodgkin's lymphoma using external beam radiotherapy (33).

In the 13 NHL patients that had initial spleen volume of 380-1400 mL, 13 patients showed splenic volume decrease after RIT (Table 2). However, the remaining 3 patients had splenic volume increase after receiving a relative low radiation dose to the spleen (1.0-3.5 Gy). Two of them showed splenic volume increase of 8% and 10% were partial-responders (PR). The third patient, who had 220% increase in splenic volume, was a non-responder (NR). This is consistent with the general observation that tumor response was more likely in patients with splenic volume decrease (Fig 2).

The use of MIRD S values based on population-averaged organ masses (mathematical phantom of reference man) provides a convenient approach for computation of radiation dose for individual patients. However, the use of fixed organ dimensions can introduce substantial deviation in radiation dose estimates as organ size can vary substantially among patients. Accurate dosimetry requires patient-specific organ mass. Using the sum-of areas method for CT sections of 10-mm thickness, Breiman et al(17) reported a mean error of 4.95 % ($\pm 2.61\%$) for phantoms ranging from 200 to 1000 ml, and a mean error of 3.59 % ($\pm 4.5\%$) for 8 spleens ranging from 309 to 3675 ml. Furthermore, Breiman et al found a mean error of 3.65% for these patients using CT scan at 20-mm slice thickness, suggesting that the problem of partial volume was not significant for spleen at 20-mm slice thickness(17). As CT slices in the present study were either 5 or 10-mm thickness, the accuracy of spleen volume measurement should

be comparable to that of Breiman et al.

Patient-specific dosimetry is best calculated using Monte Carlo or dose-kernel convolution techniques based on CT and SPECT data(34-36). These techniques are not now generally available at clinical sites. One of the difficulties in patient-specific dose calculation is to estimate photon dose contribution from other source organs without a 3-D data set. One practical solution is to include all source organs other than the target (spleen) in the remainder of the body(27). First, in 59 lymphoma patients receiving ^{131}I or ^{67}Cu , the deviation introduced by including all sources other than spleen in the remainder of the body was inconsequential (mean 0.2%, range 0.0-0.6%)(27). Therefore, the task of $S(\text{target} \leftarrow \text{other source})$ computation was simplified to $S(\text{spleen} \leftarrow \text{TB})$ computation (Equation 2). Second, despite the large mass difference between liver, spleen and kidneys, the MIRD values for $S(\text{spleen} \leftarrow \text{TB})$, $S(\text{liver} \leftarrow \text{TB})$ and $S(\text{kidneys} \leftarrow \text{TB})$ are almost identical for ^{131}I and ^{67}Cu (6,7). Therefore, $S(\text{spleen} \leftarrow \text{TB})$ value is not sensitive to the spleen mass but is sensitive to body mass. Third, despite the large mass difference between the adult phantom of 70 kg weight, the child phantom of 58 kg weight and the child phantom of 15 kg weight, the ratio of $S(\text{spleen} \leftarrow \text{TB})$ value to $S(\text{TB} \leftarrow \text{TB})$ value were all about 1.07 for ^{131}I and 1.04 for ^{67}Cu (7). As $S(\text{spleen} \leftarrow \text{TB})$ can be calculated as 1.07 $S(\text{TB} \leftarrow \text{TB})$ for ^{131}I and 1.04 $S(\text{TB} \leftarrow \text{TB})$ for ^{67}Cu , the task of patient-specific $S(\text{target} \leftarrow \text{other source})$ computation becomes patient-specific $S(\text{TB} \leftarrow \text{TB})$ computation that can be readily calculated using Equation 3.

CONCLUSION

Splenic volume changes were found in lymphoma patients with enlarged spleen. The decrease in splenic volume after RIT seemed related to therapeutic effect on malignant lymphocytes associated with splenomegaly. Nodal tumor response was more likely in those NHL patients with greater splenic volume decrease after RIT. RIT seems benefit to NHL patients with splenomegaly.

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Table 1

29 non-Hodgkin's lymphoma and 9 breast cancer patients* had CT abdomen images before and after radioimmunotherapy.

Radiopharmaceuticals	Disease	Number of Patients	Number of doses/patient (range)	Range of total radioactivity/patient (GBq)
¹³¹ I-Lym-1	NHL	25	1-13	1.74- 27.16
⁶⁷ Cu-2IT-BAT-Lym-1	NHL	4	2-3	3.74-6.55
⁹⁰ Y-MX-DTPA-BrE 3 or ⁹⁰ Y-2IT-BAD-m170	Breast cancer	3	1-3	0.41-2.00
¹³¹ I-ChL6/L6	Breast cancer	6	2-3	6.25-30.90

*: As a reference group. Spleens are expected to be no malignancy involved.

Table 2. Splenic volume change in response to RIT.

Patients	Initial splenic volume (ml)	Mean (range) splenic dose (Gy)	Mean (range) volume change after RIT (mL)
16 NHL patients			
13 NHL	380 to 1400	3.6 (1.1 to 7.0)	-186 (-68 to -548)
3 NHL	340 to 700	2.2 (1.0 to 3.5)	542 (35 to 1535)
13 NHL patients	150 to 310	8.0 (1.2 to 11.4)	-2 (-23 to 15)
9 breast cancer*	70 to 340	11.5 (1.9 to 14.4)	1 (-5 to 13)

*: As a reference group. Spleens are expected to be no malignancy involved.

Table 3. Planar image assessment for splenic volume change during sequential planar imaging. 10 NHL patients who had CT splenic volume change >15% were assessed.

NHL Patients	Duration of sequential imaging	Planar splenic volume change (%)
No.1	Immediate-264 hr	2.9
No.2	Immediate-240 hr	3.4
No.3	Immediate-144 hr	7.0
No.4	Immediate-144 hr	7.3
No.5	Immediate-144 hr	2.5
No.6	Immediate-144 hr	-2.9
No.7	Immediate-144 hr	8.7
No.8	Immediate-144 hr	10.2
No.9	Immediate-72 hr*	2.4
No.10	Immediate-120 hr	5.5

*: Image contrast was poor after 96 hours. During 72 hours, 96% of radiation dose was deposited to the spleen.

Table 4

Mass and patient-specific absorbed dose for total body and spleen.

Treatment study	Mean (range) body weight in kg	Mean (range) body absorbed dose in Gy/GBq	Mean (range) splenic volume in ml before RIT	Mean (range) splenic absorbed dose in Gy/GBq
⁹⁰ Y-MX-DTPA-BrE3 or 2IT-BAD-m170	56.8 (50.7-68.2)	0.69 (0.58-0.84)	150 (70-320)	4.67 (2.16-6.29)
¹³¹ I-ChL6/L6	65.4 (52.7-80.8)	0.24 (0.13-0.33)	230 (130-340)	0.88 (0.47-1.36)
¹³¹ I-Lym- 1	81.4 (49-146)	0.10 (0.05-0.22)	420 (140-2240)	0.53 (0.16-1.91)
⁶⁷ Cu-2IT-BAT-Lym-1	84 (70-92)	0.09 (0.08-0.10)	630 (160-1340)	0.65 (0.25-1.05)

Figure Legend

- Figure 1. In the 29 NHL patients, splenic volume change after RIT was more likely in patients with enlarged spleen.
- Figure 2. In the 29 NHL patients, nodal tumor response was more likely in those patients with greater splenic volume decrease after RIT.
- Figure 3. Patient-specific $S(\text{spleen} \leftarrow \text{spleen})$ value (rad/ $\mu\text{Ci-hr}$) in 25 NHL patients receiving ^{131}I -Lym-1 (Equation 4). Substantial deviation from the actual spleen to spleen dose would be introduced if a fixed $S(\text{spleen} \leftarrow \text{spleen})$ value of 2.6×10^{-3} (rad/ $\mu\text{Ci-hr}$) from MIRD No. 11 or 2.57×10^{-3} (rad/ $\mu\text{Ci-hr}$) from MIRDOS III program based on MIRD spleen phantom of 173.6g were used.

Fig 1

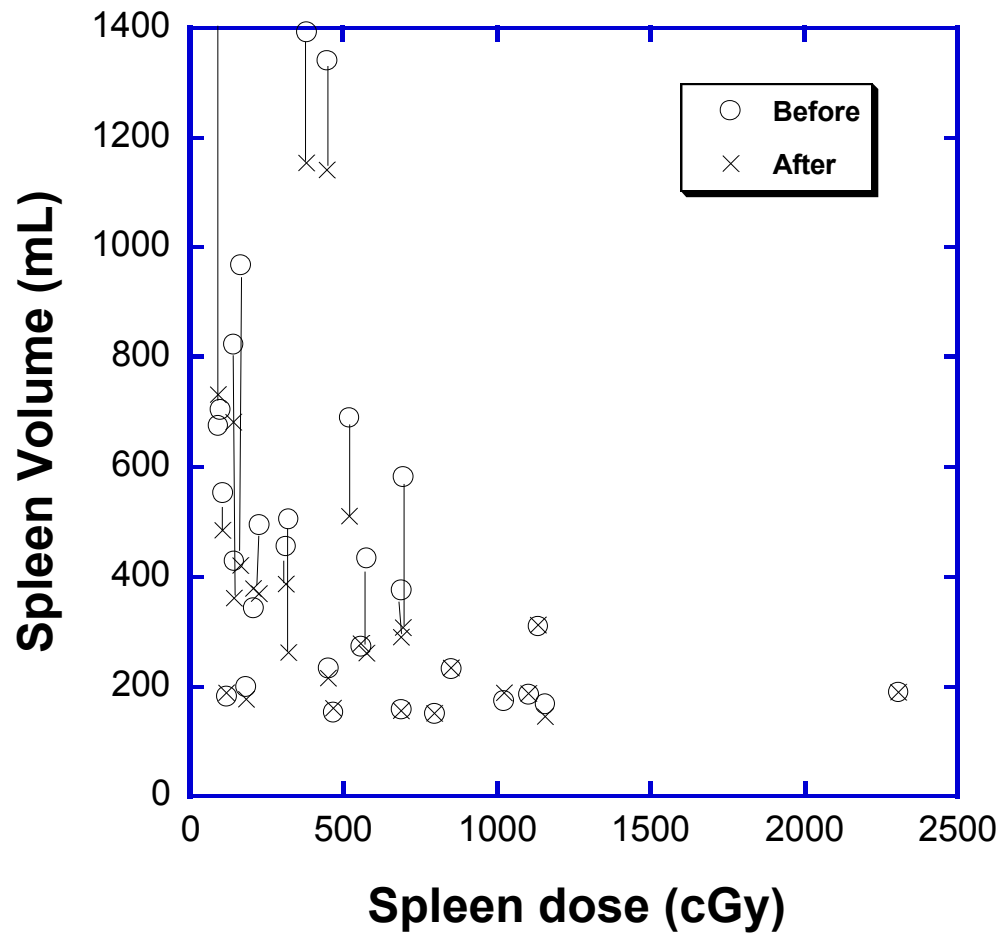


Fig 2

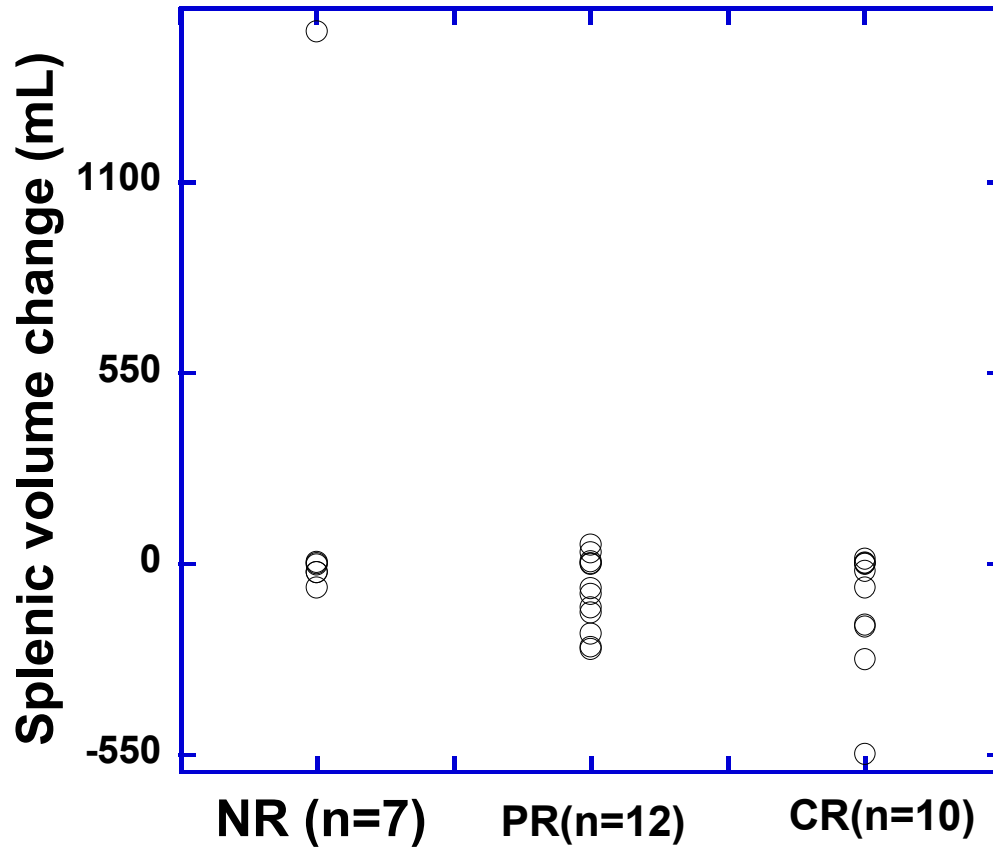
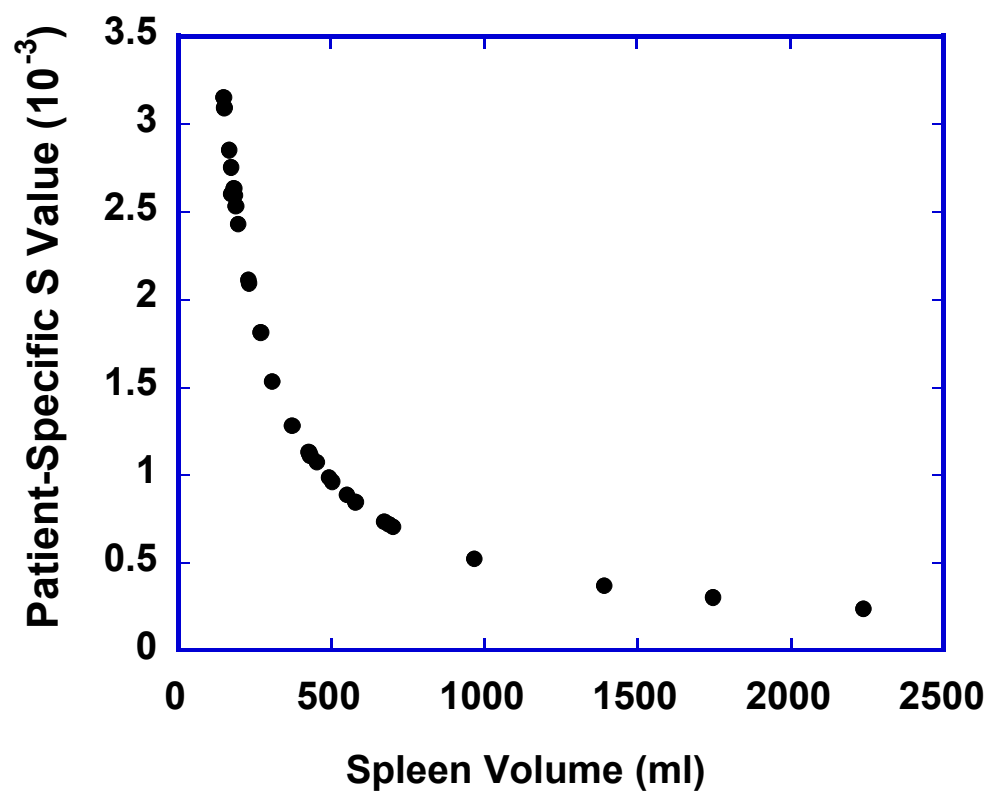


Fig 3



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